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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/564,451

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Dennis Lee

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11/08/2007

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EXAMINER

YOUNG, SHAWQUIA

ART UNIT

PAPER NUMBER

1626

NOTIFICATION DATE

DELIVERY MODE

11/08/2007

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary

Application No.

10/564,451

Applicant(s)

LEE ET AL.

Examiner

Shawquia Young

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 5-8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 1/12/06; 5/21/07.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are currently pending in the instant application.

I. *Priority*

The instant application is a 371 of PCT/US04/22706, filed on July 15, 2004, which claims benefit of US Provisional Application 60/6487,492, filed on July 15, 2003.

II. *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on January 12, 2006 is not in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has not been considered by the examiner.

The information disclosure statement (IDS) submitted on May 21, 2007 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

III. *Restriction/Election*

A. Election: Applicant's Response

Applicants' election with traverse of Group I in the reply filed on August 20, 2007 is acknowledged. The traversal is on the ground(s) that: (1) the claims have unity of invention and (2) there is no search burden for the Examiner to examine the all of the instant claims.

All of the Applicants' arguments have been considered but have not been found persuasive. It is pointed out that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to restrict

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applications to several claimed inventions when those inventions are found to be independent and distinct. The Examiner has indicated that more than one independent and distinct invention is claimed in this application and has restricted the claimed subject matter accordingly.

Applicants argue that the present invention is directed in part to a method of treating or inhibiting disorders associated with the activation of large conductance calcium activated potassium channels by administering a compound of Formula (I), which have a common utility as BK channel activators and as a whole have structural core similarity. Applicants further argue that claims 1-4, have a significant structural element qualifying as a special technical feature that defines a contribution over the prior art. However the Examiner wants to point out that Applicants special technical feature is the compound of formula I because that is what links all of the claims together. The special technical feature remains constant among all of the instant claims, therefore the variables are not included in the special technical feature. Applicants "special technical feature" is known in the art as mentioned in the previous Office action and thus does not define a contribution over the prior art (See JP 56-135404, compound 1, 2,3, etc., for example).

Applicants argue that the Examiner has not provided evidence to show why a serious search burden would be imposed upon examination of the claimed invention and/or why specific groups are unrelated because of different utilities, when the common technical feature of the claimed invention is a method of use directed to treating or inhibiting disorders associated with the activation of large conductance

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calcium activated potassium channels. However, the Examiner wants to point out that there would be a serious search and examination burden because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (d) the prior art applicable to one invention would not likely be applicable to another invention.

The Restriction Requirement detailed the reasons for restriction between the groups. Different search considerations are involved (i.e., class/subclass searches, databases searches, etc.) for each of the groups listed. The inventions are classified into classes 514, 544, 546, 548 and 549. However, each Class 514, 544, 546, 548 and 549 encompasses numerous patents and published applications. For instance, Class 514 contained 165,171 patents and published applications. Therefore it would constitute a burden on the Examiner and the Patent Office's resources to examine the instant application in its entirety.

The Examiner has agreed to expand the scope of Group I to also include wherein R_3 includes the heterocyclic groups in the definition.

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Subject matter not encompassed by elected Group I and the included above subject matter are withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to nonelected inventions.

IV. Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, while the specification provides enablement for a method of treating urinary incontinence or overactive bladder, but does not provide enablement for a method of treating or inhibiting any disorder associated with the activation of large conductance calcium activated potassium channels. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,

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2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

Applicants are claiming a method of treating or inhibiting disorders associated with the activation of large conductance calcium activated potassium channels, which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I). See, for example, instant claims 1-4.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmaceutical art, for example, remain highly unpredictable. Enablement for the scope of treating or inhibiting disorders associated with the activation of large conductance calcium activated potassium channels. is not present in the specification.

According to the specification, the disorders treatable by the instant compounds include cerebral infarction, dementia, Alzheimer's disease, Parkinson's disease, hypertension, etc.

Applicants' claims are therefore drawn to a method for treating or inhibiting

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Alzheimer's disease. It is the state of the art that there is no known cure or prevention for Alzheimer's disease and that there are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease.

(<http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html>.)

In addition, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic agents (See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, page 1994).

Applicants' claims are also drawn to a method for treating or inhibiting dementia. Dementia is the progressive decline in cognitive function due to damage or disease in the brain beyond what might be expected from normal aging. Symptoms of dementia can be classified as either reversible or irreversible depending upon the etiology of the disease. Dementia can be caused by various types of conditions or diseases, such as Alzheimer's disease, Binswanger's disease, Pick's disease, Parkinson's disease, etc. It is known (see <http://en.wikipedia.org/wiki/Dementia>) that less than 5% of a

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sample of dementia cases have a potentially treatable cause that include hypothyroidism, vitamin B1 deficiency, depressive pseudodementia, etc. Except for the treatable types of dementia, there is no cure to the illness. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the numerous diseases or disorders claimed herein. That a single class of compounds can be used to treat or control all diseases embraced by the claims is an incredible finding for which Applicants have not provided supporting evidence. Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating or inhibiting any or all conditions by administering the instant claimed compounds.

The breadth of the claims

The breadth of the claims is a method of treating or inhibiting disorders associated with the activation of large conductance calcium activated potassium channels, which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I).

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The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities for each of the diseases and disorders instantly claimed. The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to testing all diseases and disorders generically embraced in the claim language, and when faced with the unpredictability of the pharmaceutical art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the unpredictable nature of the invention and state of the prior art and lack of guidance and direction, one skilled in the art could not use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 is a composition claim that depends on a method

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claim.

V. *Objections*

Dependent Claim Objections

Dependent Claims 1-4 are also objected to as being dependent upon a rejected based claim. To overcome this objection, Applicant should rewrite said claims in an independent form and include the limitations of the base claim and any intervening claim.

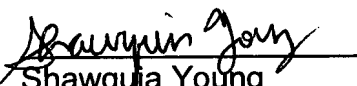
VI. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 6:30 AM-3:00PM.

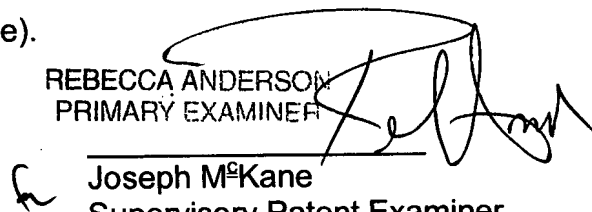
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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